

Supplementary Material

1 Supplementary Data

Genomic background characterization

In order to minimize the possible confounding effects of multiple recurrent aberrations within each sample and to establish that the analyzed patients carried only one of the aberrations of interest, we had selected cases that had been previously examined through comprehensive genomic characterization (including FISH, SNP arrays, gene panels and WES).

In more details:

1. To detect gene mutations, a previously published custom Agilent HaloPlex High Sensitivity (HS) panel design was modified using the Agilent SureDesign software (Agilent Technologies, USA).(1) The custom probes were designed to target the coding exons or hotspot regions of 13 genes of interest in CLL (*ATM*, *BIRC3*, *BTB*, *EGR2*, *FBXW7*, *MYD88*, *NFKBIE*, *NOTCH1*, *PLCG2*, *POT1*, *SF3B1*, *TP53* and *XPO1*). Libraries were prepared following the manufacturer's instructions and paired-end sequencing (150 bp reads) was performed on an Illumina's platform NextSeq500 (Illumina, San Diego, CA).
2. To detect the 2-base pair frameshift deletion in *NOTCH1*, exon 34 was amplified by PCR and then sequenced by Sanger sequencing following a previously published protocol.(2) Similarly, exons 4-8 of *TP53* gene were amplified by PCR and Sanger sequenced, as published previously.(3)
3. Whole exome sequencing (WES) libraries were prepared using TruSeq Exome Library Prep kit (Illumina, San Diego, CA) by the manufacturer's instructions. Sequencing experiments were carried out on Illumina's platform NextSeq500 following a paired-end sequencing protocol (Illumina, San Diego, CA). WES analysis performed by an in-house established computational pipeline, employing baw, sambamba and samtools consecutively.
4. Recurrent genomic aberrations were investigated also using Affymetrix GeneChip® Mapping Nsp1-250K arrays (Gene Chip Mapping 500K Assay Manual [P/N 701930 Rev2.], Affymetrix Inc., Santa Clara, CA, USA) according to the standard protocol.(4)
5. Chromosome banding analysis (CBA) and interphase fluorescence in situ hybridization (FISH) with probes for the detection of deletions of 6q21, 11q22 (*ATM*), 13q14 (*D13S25* and *D13S319*), 17p13 (*TP53*), trisomy 12 and *IGH* rearrangements were performed as previously described.(5) CBA results reported according to the International System for Human Cytogenomic Nomenclature.
6. Array CGH analyses were carried out using 4x180K microarray slides (Agilent Technologies, Santa Clara, CA). Preparation of the microarray sample assay was performed as recommended by the manufacturer. Images were analyzed using the DEVA v1.2.1 (Roche NimbleGen Inc.) and Nexus Copy Number 6.1 (Biodiscovery, Inc., El Segundo, CA). Aberrations were evaluated in each sample using BioDiscovery's Fast Adaptive States Segmentation Technique (FASST2) algorithm. Copy number changes smaller than 50 kb, as well as alterations covered by a known Copy Number Variation in the database of genomic variants, or alterations located in non-coding regions were not reported.(6)

Next-generation sequencing: library preparation, analysis and interpretation

Targeted amplification of the TRBV-TRBD-TRBJ rearrangements in all samples was performed using TCRB Gene Clonality Assay—Gel Detection (Invivoscribe, San Diego, CA, USA) and the NGS libraries were prepared based on the NEBNext® Ultra™ II DNA Library Prep Kit for Illumina (New England Biolabs Ipswich, MA, USA), as previously described.(7) The NGS libraries were sequenced on the Illumina® MiSeq platform using the MiSeq® Reagent Kit v3 (Illumina, San Diego, CA, USA). A paired-end sequencing protocol was followed in order to achieve double coverage in the TRB complementarity-determining region 3 (TRB CDR3) for each amplicon, thus increasing the accuracy of the results.

The basic steps of the bioinformatics analysis on the results of the NGS experiments included: (i) the assessment of the raw sequencing reads, (ii) the merge of paired-end reads, (iii) the annotation of the TRBV-TRBD-TRBJ gene rearrangements, and (iv) the clonotype computation followed by the meta-data interpretation.

In more detail, using the standard Illumina signal-processing software implemented by default on the sequencing platform low-quality sequences and/or sequences with unacceptable high error rate were filter-out. On the same time, all indexed reads were assigned to samples. The paired-end reads acquired during the sequencing were further characterized by a purpose-built algorithm performing: (i) length and quality filtering of raw reads, (ii) merging of filtered-in paired reads via local alignment, and (iii) length and quality filtering of the final, full-length sequences that fulfilled all the previous criteria. No base calls of Q-score<30 were allowed in the 75-nucleotide stretch upstream of the GXG motif in FR4, thus further increasing the CDR3 sequencing reliability.(8) Sequence rearrangements meeting the aforementioned criteria annotated by the IMGT/HighV-QUEST tool (<http://www.imgt.org>) and the metadata were processed by the T cell Receptor/Immunoglobulin Profiler (TRIP) analytical toolbox designed for immunogenetics analysis.(9,10) The main steps of results interpretation by TRIP consisted of selection of TRBV-TRBD-TRBJ rearrangements based on their functionality, clonotype computation, TRBV/ TRBD/ TRBJ gene repertoires extraction and cross-sample comparisons.

2 Supplementary Tables and Figures

Supplementary Tables

Supplementary table 1: Demographic and clinicobiological characteristics of the study group. | WES: whole genome sequencing, SS: Sanger sequencing for *TP53* and *NOTCH1* genes, SNP: single nucleotide polymorphism, NA: Not available

ID	Sex	IGHV gene	IGHV region Identity %	Genomic aberration	Method of detection of genomic aberrations					
					WES	Targeted panel	SS	FISH	Array-CGH	SNP arrays
Pt1	M	IGHV4-59*01	100	trisomy 12	X		X	X		
Pt2	M	IGHV4-39*06	99.6	trisomy 12	X		X	X		
Pt3	M	IGHV3-33*01	100	TP53 mutation	X		X	X		
Pt4	M	IGHV4-34*02	91.93	del(13q)	X		X	X		
Pt5	F	IGHV1-69*01	100	del(11q)	X		X	X		
Pt6	M	IGHV4-59*02	87	del(13q)	X		X	X		
Pt7	M	IGHV4-34*01	92.98	del(13q)	X		X	X		
Pt8	F	IGHV4-34*02	97.16	del(13q)	X		X	X		
Pt9	M	IGHV1-24*01	98.9	del(11q)	X		X	X		
Pt10	M	IGHV1-69*01	100	trisomy 12	X		X	X		
Pt11	M	IGHV5-51*01	100	trisomy 12	X		X	X		
Pt12	M	IGHV7-4-1*02	100	trisomy 12	X		X	X		
Pt13	M	IGHV1-69*12	100	del(11q)	X		X	X		
Pt14	F	IGHV3-53*01	100	TP53 mutation		X		X		
Pt15	F	IGHV3-15*01	100	NOTCH1 mutation		X		X		
Pt16	F	IGHV4-34*01	100	NOTCH1 mutation		X		X		
Pt17	F	NA	NA	trisomy 12		X		X		
Pt18	M	NA	NA	trisomy 12		X		X		
Pt19	M	IGHV3-23*04	95.10	trisomy 12		X		X		
Pt20	F	IGHV1-69*01	100	trisomy 12		X		X	X	
Pt21	M	IGHV3-72*01	99.13	TP53 mutation		X		X	X	
Pt22	M	IGHV3-11*01	91.67	TP53 mutation		X		X	X	
Pt23	F	IGHV2-5*06	95.53	NOTCH1 mutation		X		X	X	
Pt24	F	IGHV3-7*01	91.74	NOTCH1 mutation		X		X	X	

					Method of detection of genomic aberrations					
ID	Sex	IGHV gene	IGHV region Identity %	Genomic aberration	WES	Targeted panel	SS	FISH	Array-CGH	SNP arrays
Pt25	F	IGHV3-23*01	93.33	trisomy 12		X		X	X	
Pt26	F	IGHV1-8*01	93.4	TP53 mutation		X		X	X	
Pt27	M	IGHV3-30*02	100	NOTCH1 mutation		X		X	X	
Pt28	M	IGHV3-30*03	91.51	del(13q)			X			X
Pt29	M	IGHV3-48*03	100	trisomy 12			X			X
Pt30	M	IGHV4-b	100	trisomy 12			X			X
Pt31	F	IGHV3-72*01	97.01	trisomy 12			X			X
Pt32	M	IGHV3-48*03	97.77	del(13q)			X			X
Pt33	M	IGHV4-34*01	99.56	del(11q)			X			X
Pt34	F	IGHV3-15*07	92.83	del(11q)			X			X
Pt35	F	IGHV3-9*01	93.01	del(13q)			X			X
Pt36	F	IGHV3-15*01	100	trisomy 12			X			X
Pt37	M	IGHV3-21*01	100	trisomy 12			X			X
Pt38	M	IGHV4-39*01	96.63	del(11q)			X			X
Pt39	F	IGHV3-30-3*01	100	del(11q)			X			X
Pt40	M	IGHV1-69*01	100	del(11q)			X			X
Pt41	M	IGHV1-69*01	100	trisomy 12			X			X
Pt42	F	IGHV3-11*01	100	trisomy 12			X			X
Pt43	F	IGHV3-30*18	97.64	del(11q)			X			X
Pt44	M	IGHV3-21*01	98.67	del(11q)			X			X

Supplementary table 2: Overall metrics of the NGS data.

Group	Median number of raw reads/sample	Median number of productive sequences/sample	Range	Median number of distinct clonotypes/sample	Range
del(11q)	299,237	220,553	124,930 - 261,880	7,831	2,545 - 21,815
del(13q)	255,988	181,574	33,493 - 255,256	11,056	3,419 - 18,753
trisomy 12	293,122	215,356	44,132 - 293,869	10,608	2,325 - 26,719
<i>NOTCH1</i> mutation	274,370	222,138	131,040 - 225,940	10,132	7,578 - 21,725
<i>TP53</i> mutation	300,490	183,371	115,829 - 256,024	8,567	3,530 - 23,986

Supplementary table 3: Significantly expanded clonotypes. The number of clonotypes per sample that presented with frequency above 0.216% and considered as significantly expanded.

Manuscript ID	Genomic aberration	No of expanded clonotypes (f>0.216%)
Pt1	trisomy 12	17
Pt2	trisomy 12	11
Pt3	TP53 mutation	17
Pt4	del(13q)	12
Pt5	del(11q)	28
Pt6	del(13q)	14
Pt7	del(13q)	10
Pt8	del(13q)	10
Pt9	del(11q)	5
Pt10	trisomy 12	31
Pt11	trisomy 12	20
Pt12	trisomy 12	21
Pt13	del(11q)	13
Pt14	TP53 mutation	10
Pt15	NOTCH1 mutation	12
Pt16	NOTCH1 mutation	9
Pt17	trisomy 12	16
Pt18	trisomy 12	17
Pt19	trisomy 12	19
Pt20	trisomy 12	15
Pt21	TP53 mutation	7
Pt22	TP53 mutation	26
Pt23	NOTCH1 mutation	14
Pt24	NOTCH1 mutation	17
Pt25	trisomy 12	13
Pt26	TP53 mutation	24
Pt27	NOTCH1 mutation	9
Pt28	del(13q)	5
Pt29	trisomy12	18
Pt30	trisomy12	20
Pt31	del(13q)	22
Pt32	del(13q)	27
Pt33	del(11q)	29
Pt34	del(13q)	23
Pt35	del(13q)	20
Pt36	trisomy12	19
Pt37	trisomy12	27
Pt38	del(11q)	15
Pt39	del(11q)	27
Pt40	del(11q)	22
Pt41	trisomy12	23
Pt42	trisomy12	13
Pt43	del(11q)	13
Pt44	del(11q)	25

Supplementary table 4: Tumor-derived epitopes for each case bearing *TP53* or *NOTCH1* mutations. Complete lists with the predicted tumor epitopes derived from a particular lesion on *TP53* or *NOTCH1*.

Case ID	Gene	Variant name	Molecular consequence	No of predicted neo-epitopes
Pt3	TP53	NM_000546.6:c.100C>T p.Pro34Ser	Substitution - Missense	19
LSSLPSQAM	VLSSLPSQAMDD	LSSLPSQAMDDL	LSSLPSQAMDDLML	LSSLPSQAMDDLMLS
VLSSLPSQAM	SSLPSQAMDDL	SSLPSQAMDDLML	SSLPSQAMDDLMLS	SSLPSQAMDDLMLSP
VLSSLPSQAMD	SLPSQAMDDLML	SLPSQAMDDLMLS	SLPSQAMDDLMLSP	SLPSQAMDDLMLSPD
SLPSQAMDDL	VLSSLPSQAMDDL	VLSSLPSQAMDDL	VLSSLPSQAMDDLML	
Pt14	TP53	NM_000546.6:c.733G>A p.Gly245Ser NM_000546.6:c.1146del p.Lys382fs	Substitution - Missense Deletion/Insertion - Frameshift	182
YNYMCNSSC	SKKGQSTSR	TSRHKKLMFK	CNSSCMGSMNRR	TSSSPQPKKKPLD
NYMCNSSCM	STSRHKKLM	SRHKKLMFKT	NSSCMGSMNRRP	SSSPQPKKKPLDG
YMCNSSCMG	SRHKKLMFK	YNYMCNSSCMG	VRVCACPGRRR	RGRERFEMFREL
MCNSSCMGS	RHKKLMFKT	NYMCNSSCMGS	GRDRRTEENLR	KSKKGQSTSRHKK
CNSSCMGSM	YNYMCNSSCM	YMCNSSCMGSM	RDRRTEENLRK	YMCNSSCMGSMNRR
SSCMGSMNR	NYMCNSSCMG	MCNSSCMGSMN	DRRTEENLRKK	MCNSSCMGSMNRRP
SCMGSMNRR	YMCNSSCMGS	CNSSCMGSMNR	RRTTEENLRKKG	PGDRRTEENLRK
CMGSMNRRP	MCNSSCMGSM	NSSCMGSMNRR	RKKGEFHHELPP	GRDRRTEENLRKK
MGSMNRRPI	CNSSCMGSMN	SSCMGSMNRRP	LPFGSTKRALPN	RDRRTEENLRKKG
GSMNRRPIL	SSCMGSMNRR	NLLGNSFEVR	FPFGSTKRALPNN	LPFGSTKRALPNT
SMNRRPILT	SCMGSMNRRP	SFEVRVCACPG	FPFGSTKRALPNT	FPFGSTKRALPNTS
LGRNSFEVR	MGSMNRRPIL	FEVRVCACPGR	KRALPNTSSSP	KRALPNTSSSPQ
GRNSFEVRV	NSFEVRVCAC	EVVRVCACPGD	LPNNTSSSPQPK	RALPNTSSSPQPK
SFEVRVCAC	SFEVRVCACP	VRVCACPGRR	PNNTSSSPQPKK	ALPNTSSSPQPKK
FEVRVCACP	FEVRVCACPG	RDRRTEENLR	NNTSSSPQPKKK	LPNNTSSSPQPKK
EVVRVCACPG	EVVRVCACPGR	RRTTEENLRKK	NTSSSPQPKKKP	PNNTSSSPQPKKK
VRVCACPGR	VRVCACPGRD	KKGEFHHELPP	TSSSPQPKKKPL	NNTSSSPQPKKKPL
RVCACPGRD	RRTTEENLRK	LPFGSTKRALP	SSSPQPKKKPLD	NTSSSPQPKKKPLD
VCACPGRR	NLRKKGEPIH	PPGSTKRALPN	SSPQPKKKPLDG	TSSSPQPKKKPLDG
RDRRTEEN	PPGSTKRALP	PGSTKRALPNN	QIRGRERFEMFR	LKSKKGQSTSRHKK
RRTTEENLR	PGSTKRALPN	KRALPNTSSS	RGRERFEMFREL	KSKKGQSTSRHKKL
NLRKKGEPIH	GSTKRALPNN	PNNTSSSPQPK	KSKKGQSTSRHK	PGDRRTEENLRKK
RKKGEPIHE	STKRALPNT	NNTSSSPQPKK	KSKKGQSTSRHKK	GRDRRTEENLRKKG
STKRALPNN	TKRALPNTS	NTSSSPQPKKK	KKKGQSTSRHKKL	PPGSTKRALPNTSS
TKRALPNT	KRALPNTSS	TSSSPQPKKKP	YNYMCNSSCMGSM	TKRALPNTSSSPQ
KRALPNTS	PNNTSSSPQ	SSSPQPKKKPL	YMCNSSCMGSMNR	KRALPNTSSSPQ
NTSSSPQPK	NNTSSSPQPK	SSPQPKKKPLD	MCNSSCMGSMNRR	RALPNTSSSPQPK
TSSSPQPKK	NTSSSPQPKK	SPQPKKKPLDG	PGDRRTEENLR	ALPNTSSSPQPKK
SSSPQPKKK	TSSSPQPKKK	IRGRERFEMFR	GRDRRTEENLRK	LPNNTSSSPQPKK
SSPQPKKKP	SSPQPKKKP	RGRERFEMFRE	RDRRTEENLRKK	PNNTSSSPQPKKK
SPQPKKKPL	SSPQPKKKPL	KSKKGQSTSRH	LPFGSTKRALPNN	NNTSSSPQPKKKPL
PQPKKKPLD	SPQPKKKPLD	KSKKGQSTSRHK	PPGSTKRALPNT	NTSSSPQPKKKPLDG
TLQIRGRER	PQPKKKPLDG	KKGQSTSRHKK	TKRALPNTSSSP	HLKSKKGQSTSRHKK
LQIRGRERF	RGRERFEMFR	YNYMCNSSCMGS	LPNNTSSSPQPKK	KSKKGQSTSRHKKLM
IRGRERFEM	KSKKGQSTSR	NYMCNSSCMGSM	PNNTSSSPQPKK	
RGRERFEMF	KKGQSTSRHK	YMCNSSCMGSMN	NNTSSSPQPKKKP	
GRERFEMFR	KQGSTSRHKK	MCNSSCMGSMNR	NTSSSPQPKKKPL	
Pt21	TP53	NM_000546.6:c.464C>A p.Thr155Asn	Substitution - Missense	28
WVDSTPPPG	PPGNRVVRAM	TPPPGNRVRA	TPPPGNRVVRAM	CPVQLWVDSTPPPG
VDSTPPPGN	LWVDSTPPPG	PPPGNVVRAM	VQLWVDSTPPPG	EVQLWVDSTPPPGN
DSTPPPGNR	WVDSTPPPGN	QLWVDSTPPPG	VDSTPPPGNRVR	TCFVQLWVDSTPPPG
STPPPGNRV	VDSTPPPGNR	LWVDSTPPPGN	DSTPPPGNRVRA	CPVQLWVDSTPPPGN
TPPPGNRVVR	DSTPPPGNRV	DSTPPPGNRVR	STPPPGNRVRAM	
PPPGNRVRA	STPPPGNRVR	STPPPGNRVRA	EVQLWVDSTPPPG	
Pt22	TP53	NM_000546.6:c.607G>C p.Val203Leu	Substitution - Missense	1
LIRVEGNLRL				
Pt23	NOTCH1	NM_017617.5:c.7541_7542del p.Pro2514fs	Deletion - Frameshift	3
PEHPFLTPS	PFLTPSRVP	PEHPFLTPSRVP		
Pt24	NOTCH1	NM_017617.5:c.7541_7542del p.Pro2514fs	Deletion - Frameshift	3
PEHPFLTPS	PFLTPSRVP	PEHPFLTPSRVP		
Pt26	TP53	NM_000546.6:c.721T>C p.Ser241Pro	Substitution - Missense	20
NYMCNSPCM	YNYMCNSPCM	CNSPCMGGMN	MCNSPCMGGMN	MCNSPCMGGMNR
YMCNSPCM	NYMCNSPCM	YNYMCNSPCM	YNYMCNSPCMGG	YNYMCNSPCMGGM
MCNSPCMGG	YMCNSPCMGG	NYMCNSPCMGG	NYMCNSPCMGGM	YMCNSPCMGGMNR
CNSPCMGGM	MCNSPCMGGM	YMCNSPCMGGM	YMCNSPCMGGMN	MCNSPCMGGMNR
Pt27	NOTCH1	NM_017617.5:c.7541_7542del p.Pro2514fs	Deletion - Frameshift	3
PEHPFLTPS	PFLTPSRVP	PEHPFLTPSRVP		

Supplementary table 5: MHC alleles expressed in each case. Typing of the HLA-A, -B, -C (low resolution) and -DRB1 (allelic level high resolution determination) loci was performed.

ID	MHC alleles									
Pt3	HLA-A*02		HLA-B*18	HLA-B*27	HLA-C*02	HLA-C*12	HLA-DR B1*01:01	HLA-DR B1*16:01	HLA-DQ B1*05:01	HLA-DQ B1*05:02
Pt14	HLA-A*11	HLA-A*24	HLA-B*07	HLA-B*15	HLA-C*03	HLA-C*07	HLA-DR B1*07	HLA-DR B1*15		
Pt21	HLA-A*01	HLA-A*11	HLA-B*08	HLA-B*35	HLA-C*04	HLA-C*07	HLA-DR B1*01:01	HLA-DR B1*03:01	HLA-DQ B1*02:01	HLA-DQ B1*05:01
Pt22	HLA-A*02	HLA-A*32	HLA-B*39	HLA-B*44	HLA-C*12	HLA-C*16	HLA-DR B1*07:01	HLA-DR B1*11:01	HLA-DQ B1*02:02	HLA-DQ B1*03:01
Pt23	HLA-A*01		HLA-B*08		HLA-C*07		HLA-DR B1*03:01		HLA-DQ B1*02:01	
Pt24	HLA-A*03	HLA-A*33	HLA-B*27	HLA-B*35	HLA-C*02	HLA-C*04	HLA-DR B1*03:01	HLA-DR B1*15:01	HLA-DQ B1*02:01	HLA-DQ B1*06:02
Pt26	HLA-A*01	HLA-A*02	HLA-B*08	HLA-B*44	HLA-C*07		HLA-DR B1*03:01	HLA-DR B1*11:01	HLA-DQ B1*02:01	HLA-DQ B1*03:01
Pt27	HLA-A*02	HLA-A*24	HLA-B*35	HLA-B*39	HLA-C*04	HLA-C*12	HLA-DR B1*07:01	HLA-DR B1*11:01	HLA-DQ B1*02:01	HLA-DQ B1*03:03

Supplementary table 6: TRBV gene repertoire. Differential TRBV gene usage in the expanded clonotype repertoire compared to the remaining polyclonal background | logFC: a log-fold change between TRBV gene frequency of the expanded clonotype repertoire and the frequency on the remaining polyclonal background; adj.P.Val: adj.P.Value is the p-value adjusted for multiple testing following Benjamini and Hochberg's method to control the false discovery rate.

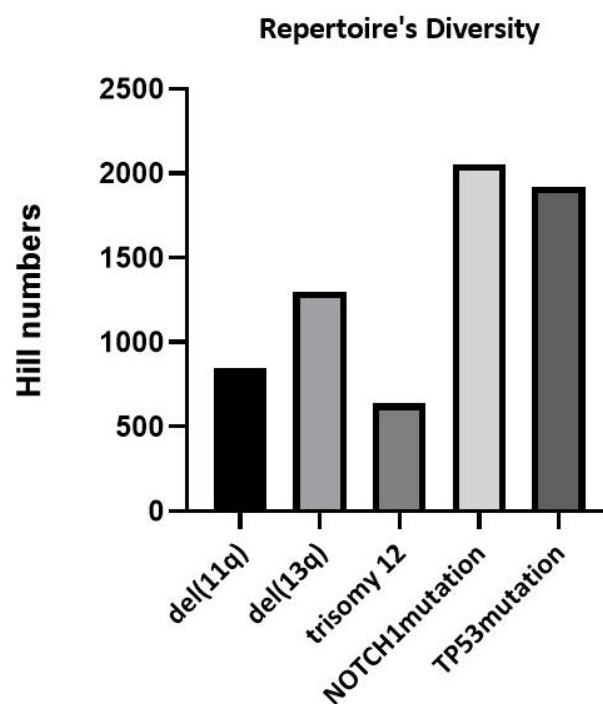
del(11q)			
Target	logFC	P.Value	adj.P.Val
TRBV29-1	9.079555	5.85E-05	0.002749
TRBV7-6	-0.55498	0.00027	0.004389
TRBV14	-0.4564	0.000319	0.004389
TRBV3-1	-0.29326	0.000414	0.004389
TRBV25-1	-0.32633	0.000467	0.004389
TRBV9	-0.2901	0.000619	0.004852
TRBV4-2	-1.0444	0.000905	0.006079
TRBV7-3	-0.61974	0.001109	0.006514
TRBV11-2	-1.36396	0.001642	0.008575
TRBV11-1	-0.54874	0.002157	0.010138
TRBV7-9	-2.12495	0.002412	0.010304
TRBV10-2	-0.31498	0.010125	0.039655
TRBV7-2	-2.27468	0.011794	0.042641

Trisomy 12			
Target	logFC	P.Value	adj.P.Val
TRBV3-1	-0.23719	2.05E-07	7.74E-06
TRBV7-3	-0.5672	4.74E-07	7.74E-06
TRBV9	-0.26562	4.94E-07	7.74E-06
TRBV25-1	-0.31109	8.32E-07	9.44E-06
TRBV11-1	-0.48803	1.00E-06	9.44E-06
TRBV7-6	-0.55604	1.13E-05	8.87E-05
TRBV29-1	9.475572	1.89E-05	0.000127
TRBV7-2	-2.25933	6.00E-05	0.000353
TRBV6-1	-1.7745	0.000286	0.001493
TRBV11-3	-0.32985	0.000659	0.003098
TRBV20-1	-1.40655	0.001038	0.004434
TRBV7-4	-0.18559	0.001276	0.005
TRBV14	-0.28954	0.003838	0.013876
TRBV12-3	5.229178	0.006635	0.022274
TRBV12-4	-0.06542	0.008174	0.025612
TRBV7-7	-0.12072	0.011758	0.034538
TRBV6-6	-1.33366	0.012888	0.035631

del(13q)			
Target	logFC	P.Value	adj.P.Val
TRBV4-2	-1.35811	8.62E-06	0.000405
TRBV6-1	-3.28612	0.000476	0.011193
TRBV5-5	-1.88811	0.000815	0.012766
TRBV7-3	-0.64304	0.001446	0.015963
TRBV7-6	-0.5054	0.001698	0.015963
TRBV11-1	-0.51566	0.00241	0.016474
TRBV12-5	-1.03945	0.002454	0.016474

NOTCH1 mutation			
Target	logFC	P.Value	adj.P.Val
TRBV7-8	-2.33367	7.58E-06	0.000356
TRBV11-2	-2.63173	3.49E-05	0.000754
TRBV20-1	-2.63856	6.39E-05	0.000754
TRBV7-2	-3.87785	6.41E-05	0.000754
TRBV2	-1.68294	0.000488	0.00431
TRBV5-5	-2.35815	0.00055	0.00431
TRBV4-2	-1.43153	0.00083	0.005023
TRBV5-4	-2.31551	0.000855	0.005023
TRBV11-1	-0.72426	0.001198	0.006254
TRBV10-2	-0.5126	0.00291	0.013677
TRBV6-6	-2.84471	0.005417	0.023144
TRBV9	-0.4499	0.006881	0.026952
TRBV5-8	-0.70809	0.007495	0.027098
TRBV7-9	-2.2199	0.010113	0.033951
TRBV25-1	-0.28645	0.012688	0.039756
TRBV29-1	18.56844	0.013623	0.040018

TP53 mutation			
Target	logFC	P.Value	adj.P.Val
TRBV7-8	-2.08169	8.82E-05	0.004146
TRBV11-3	-0.8491	0.000251	0.005893
TRBV12-3	8.674279	0.001413	0.022133
TRBV7-2	-4.00013	0.002004	0.023552
TRBV2	-1.36689	0.004243	0.039883
TRBV4-1	-1.20962	0.006009	0.047067

Supplementary Figure

Supplementary figure 1: T cell receptor gene repertoire diversity expressed as Hill numbers (¹D). Columns display the average value of Hill numbers for each group of the present study.

3 References

1. Agathangelidis A, Ljungström V, Scarfò L, Fazi C, Gounari M, Pandzic T, et al. Highly similar genomic landscapes in monoclonal B-cell lymphocytosis and ultra-stable chronic lymphocytic leukemia with low frequency of driver mutations. *Haematologica*. 2018 May 1;103(5):865 LP – 873.
2. Mansouri L, Cahill N, Gunnarsson R, Smedby KE, Tjönnfjord E, Hjalgrim H, et al. NOTCH1 and SF3B1 mutations can be added to the hierarchical prognostic classification in chronic lymphocytic leukemia. *Leukemia*. 2013 Feb;27(2):512–4.
3. Gunnarsson R, Isaksson A, Mansouri M, Göransson H, Jansson M, Cahill N, et al. Large but not small copy-number alterations correlate to high-risk genomic aberrations and survival in chronic lymphocytic leukemia: a high-resolution genomic screening of newly diagnosed patients. *Leukemia* 2010 24:1. 2009 Sep 10;24(1):211–5.
4. Gunnarsson R, Mansouri L, Isaksson A, Göransson H, Cahill N, Jansson M, et al. Array-based genomic screening at diagnosis and during follow-up in chronic lymphocytic leukemia. *Haematologica* [Internet]. 2011 Aug 1 [cited 2022 Sep 27];96(8):1161–9. Available from: <https://haematologica.org/article/view/6043>
5. Dicker F, Schnittger S, Haferlach T, Kern W, Schoch C. Immunostimulatory oligonucleotide-induced metaphase cytogenetics detect chromosomal aberrations in 80% of CLL patients: A study of 132 CLL cases with correlation to FISH, IgVH status, and CD38 expression. *Blood*. 2006 Nov 1;108(9):3152–60.
6. MacDonald JR, Ziman R, Yuen RKC, Feuk L, Scherer SW. The Database of Genomic Variants: a curated collection of structural variation in the human genome. *Nucleic Acids Res*. 2014 Jan 1;42(D1):D986–92.
7. Vlachonikola E, Vardi A, Stamatopoulos K, Hadzidimitriou A. High-Throughput Sequencing of the T-Cell Receptor Beta Chain Gene Repertoire in Chronic Lymphocytic Leukemia. In: *Methods in Molecular Biology*. Humana Press Inc.; 2019. p. 355–63.
8. Vardi A, Vlachonikola E, Karypidou M, Stalika E, Bikos V, Gemenetzi K, et al. Restrictions in the T-cell repertoire of chronic lymphocytic leukemia: High-throughput immunoprofiling supports selection by shared antigenic elements. *Leukemia*. 2017;31(7):1555–61.
9. Kotouza MT, Gemenetzi K, Galigalidou C, Vlachonikola E, Pechlivanis N, Agathangelidis A, et al. TRIP - T cell receptor/immunoglobulin profiler. *BMC Bioinformatics*. 2020 Sep 29;21(1):422.
10. Alamyar E, Duroux P, Lefranc MP, Giudicelli V. IMGT® Tools for the Nucleotide Analysis of Immunoglobulin (IG) and T Cell Receptor (TR) V-(D)-J Repertoires, Polymorphisms, and IG Mutations: IMGT/V-QUEST and IMGT/HighV-QUEST for NGS. In: *Methods in molecular biology* (Clifton, NJ). *Methods Mol Biol*; 2012. p. 569–604.